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EXAMINER	
SOUAYA, JEHANNE E	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/932,122	Applicant(s) BAKER, TONY	
	Examiner Jehanne E Souaya	Art Unit 1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *16 August 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 5, 9, 14, 21, 25, 30, 32-35, 41, 44, 46, and 47 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 5, 9, 21, 25, 41, and 44 recite "at least about". This recitation is indefinite as it is unclear if the term is meant to indicate "about 0.01" or if this recitation indicates a minimum of "about 0.01M" but no maximum, for example 2M could read on such a recitation.

B) Claims 14, 30, and 45 recite concentrations that encompass 0. Therefore, it is unclear how the test sample is further contacted with a reagent whose concentration is 0.

C) Claim 32 recites "said bodily fluid" which lacks sufficient antecedent basis as the claim is dependent from claim 20, which does not recite any bodily fluids. It appears that this claim should be dependent from claim 31.

D) Claim 46 lacks sufficient antecedent basis for the term "said nucleic acid" because it is unclear if the term refers to the nucleic acid containing test sample or the target nucleic acid of claim 37.

E) Claim 48 (dependent from claim 1) lacks sufficient antecedent basis for the term "said amplification" as no amplification is recited in claim 1.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. Claims 1-8, 14, 15, 17-24, 30, 36-43, and 45, 46, and 48 are rejected under 35 U.S.C. 102(b) as being anticipated by Chung et al (Mol Cells. Vol. 6, pp 108-111, 1996).

The claims are drawn to a method of suppressing the interference of a masking agent on a molecular assay of a nucleic acid containing test sample or a method of improving the signal response of a molecular assay by suppressing the interference of a masking agent on a molecular assay of a nucleic acid containing test sample, or a method of improving hybridization of nucleic acids comprising contacting the test sample with an amount of a divalent metal chelator and a chelator enhancing component. Claim 17 is further drawn to extracting molecular analytes of interest from the sample, and conducting a molecular assay on the extracted molecular analytes. With regard to claim 37, the recitation of "test nucleic acid" and "target nucleic acid" are interpreted to be any nucleic acid molecule, respectively

With regard to claims 1, 17, and 37, Chung et al teach an improved method of isolating quality polysaccharide free RNA from plant tissues by 1) adding an extraction buffer (buffer A; limitations of claims 2-8, 14, 18-24, 30, 38-43, and 45) comprising 300 mM (0.3M) LiCl and 10mM (0.01M) EDTA and 1.5% SDS to a sample (test sample containing nucleic acid) of pulverized sesame and perilla oilseeds (see p. 109, col. 1, "Solutions", "Procedure"), 2) extracting RNA (extracting molecular analytes of interest) (p. 109, cols 1 and 2 "procedure"),

and 3) spectrophotometrically and electrophoretically (p. 109, last para, table 1, Figure 1) assessing the quality and quantity of extracted RNA, Northern Hybridization (fig 2), and RT-PCR with the RNA (conducting a molecular assay on the extracted molecular analytes of interest). Chung specifically teaches that the quality of RNA was dependent on the RNA extraction buffer used and that buffer A greatly enhanced the RNA quality isolated from oilseeds of sesame and perilla (p. 110, col. 1, lines 1-4). Table 1 of Chung teaches enhanced absorbance ratios (improved signal response) and Figure 1 of Chung teaches clearer bands on an agarose gel with the use of buffer A. Claims 36 and 48 are drawn to the method wherein the molecular assay is PCR. Chung teaches constructing cDNA libraries from RNA populations acquired using buffer A, and that northern hybridization using cDNA probes showed that the RNA isolated was intact and functional (page 111- first para, figure 2), therefore Chung inherently teaches an RT-PCR method with improved signal (figure 2) (in this case, "signal response" is broadly interpreted to encompass intact and functional cDNA derived from isolated RNA using buffer A and "improved hybridization" is broadly interpreted to encompass Northern hybridization in figure 2 with the improved quality RNA as well as hybridization of primer to target in the RT-PCR with improved signal).

8. Claims 1-6, 8, 9, 14-22, 24, 25, 30-41, and 43-48 are rejected under 35 U.S.C. 102(b) as being anticipated by Sigman et al (WO 93/03167, 2/18/1993).

The claims are drawn to a method of suppressing the interference of a masking agent on a molecular assay of a nucleic acid containing test sample or a method of improving the signal response of a molecular assay by suppressing the interference of a masking agent on a molecular assay of a nucleic acid containing test sample, or a method of improving hybridization of nucleic

acids comprising contacting the test sample with an amount of a divalent metal chelator and a chelator enhancing component. Claim 17 is further drawn to extracting molecular analytes of interest from the sample, and conducting a molecular assay on the extracted molecular analytes. With regard to claim 37, the recitation of "test nucleic acid" and "target nucleic acid" are interpreted to be any nucleic acid molecule, respectively.

With regard to claims 1, 17, and 37, Sigman teaches a method of isolating and preserving DNA. Sigman teaches that there is a need to isolate and prevent degradation of DNA in blood samples from patients suspected of infection with parasites, such as T. Cruzi (eukaryotic DNA; claims 15-16, 34-35, and 46-47) or other infectious agents during storage (p. 3, lines 16-19). Sigman teaches that isolation and storage comprise contacting a biological sample containing DNA in cells with a buffer (aqueous solution) containing a nonamphipathic chaotropic salt (chelator enhancing component) such as guanidine thiocyanate or guanidine chloride (claims 6 and 23) and a concentration of a chelating agent (divalent metal chelator; claims 2, 3, 18, 19, 38, and 39) such as EDTA (see p. 9, lines 1-11). Sigman teaches that the method is suitable for use on any biological sample including human blood, urine, sputum and lymphatic fluid (claims 31-33) (p. 12, lines 15-21). Sigman teaches that preferably, the guanidinium chloride is present in at least 3 molar concentration (this concentration anticipates claim 8 [and 24] as the range in claim 8 recites a 20 fold difference in concentration, such that 'about' 0.1-2M is broadly interpreted to encompass 3 M; also with regard to claims 9 and 25, "at least about 1M" is interpreted to encompass a minimum of about 1M with any maximum concentration above "about 1M" which includes 3M) and the chelating agent in at least 0.1 molar concentration (claims 4, 20, and 40) in the mixture of the biological sample and storage buffer (with regard to claims 5, 21, and 41, Sigman teaches a solution that contains a divalent metal chelator in an amount of at least about

0.01M). Sigman specifically teaches that human intravenous blood was freshly drawn and added to a tube containing guanidinium chloride and EDTA so that the final concentration of each was 3M and .1M respectively (p. 26, Example 1). Sigman teaches that the DNA was extracted (extracting molecular analytes of interest) and electrophoresed (conducting a molecular assay) and that the DNA stored in a mixture of the buffer remains intact at 37 deg. C for at least a month (page 27 and Figure 1). As Sigman teaches that there is a need to prevent DNA degradation in blood samples (p. 3, lines 16-20), the method of Sigman inherently improves the signal response of the electrophoresis step taught by Sigman in example 1 as the intact DNA bands visible on the gel is an inherent improvement over the smear of DNA that would be observed should the DNA have been degraded. Preventing such degradation inherently suppresses the interference of a masking agent, such as a nuclease which would degrade the DNA. With regard to claims 36 and 48, Sigman teaches that there is a need to prepare the DNA for amplification (p. 3, lines 20-21). Sigman specifically teaches a polymerase chain reaction on cleaved minicircle DNA extracted from a blood/GnCl/ EDTA (GEB lysate) sample (see examples 3 and 4). Sigman teaches that using the GEB lysate, PCR amplification of extracted minicircles was sensitive enough that a single T.cruzi cell could be detected in 20 ml of blood (p. 35). With regard to claim 37, the method of Sigman is interpreted to improve hybridization of primers to intact DNA as compared to hybridization that would occur with regard to degraded DNA. With regard to claims 14, 30, and 45, the claims recite that the enzyme inactivating component can be present at a concentration of 0, which is anticipated by the reagent taught by Sigman.

9. Claims 1-6, 8-9, 14-16, 37-41, 43-47 are rejected under 35 U.S.C. 102(b) as being anticipated by Zhang (WO 95/35390; 12/28/1995).

The claims are drawn to a method of suppressing the interference of a masking agent on a molecular assay of a nucleic acid containing test sample or a method of improving hybridization of nucleic acids comprising contacting the test sample with an amount of a divalent metal chelator and a chelator enhancing component. With regard to claim 37, the recitation of "test nucleic acid" and "target nucleic acid" are interpreted to be any nucleic acid molecule, respectively.

With regard to claims 37-41 and 43-47, Zhang teaches a method comprising adding a lysis buffer containing 2.5-5M guanidine thiocyanate and 100mM EDTA to an equal volume of sample (eg serum) that contains nucleic acids (test nucleic acids) (it is noted that the final concentration of buffer would be 1.25-2.5 M GnSCN and .05M EDTA) (p. 14, lines 8-30), and subsequently adding nucleic acid amplification probes (target nucleic acid) and paramagnetic beads to the solution containing lysis buffer and nucleic acids from the sample. Zhang specifically teaches that hybridization occurs between the nucleic acid from the sample and the probes (p.17, lines 19-20). Zhang specifically teaches that the method can be used for detection of genetic variations in samples from patients with genetic diseases or neoplasia (page 4, lines 13-23, page 5, lines 12-19- eukaryotic DNA). It is noted that the preamble is drawn to "a method of improving hybridization of nucleic acids". However, the recitation of "improve hybridization of nucleic acids" does not carry patentable weight to overcome the teachings of Zhang as the positive process steps of the claimed method are taught by Zhang in the same order.

With regard to claim 1, Zhang teaches that the complex comprising target nucleic acid probes is separated by means of a magnetic field and that the complex is washed 2-3 times with a wash buffer comprising 1-1.5 M GnSCN and 10 mM EDTA (claims 2-6, 8-9) which removes unbound proteins, nucleic acids, and probes that may interfere with subsequent steps

(suppressing the interference of a masking agent) (see para bridging pp 17-18). With regard to claims 14, the claim recites that the enzyme inactivating component can be present at a concentration of 0, which is anticipated by the washing buffer reagent taught by Zhang.

8. Claims 1-3, 6, 10-19, 22, 26-32 and 34-36 are rejected under 35 U.S.C. 102(e) as being anticipated by Harvey et al (US Patent 6,168, 922; 102(e) date: 4/9/1997) as defined by Akane et al (Forensic Science, vol. 39, pp 362-372, 1994). (It is noted that the following rejection also applies to claims 1-3, 10, 12-19, 22, 26, 28-32, and 34-36 under 35 USC 102(a) as the claims have not been awarded the benefit of the priority of parent application 09/185,401 as the '401 application does not provide support for "suppressing a masking agent or suppressing the interference of a masking agent", or such masking agents as leukocyte esterases, and bilirubin. Claims 11 and 27 have been awarded the benefit of the filing date of the '401 application as the application states that the reagent concentrations were found to modulate the effect of hemoglobin, mathemoglobin. This disclosure does not provide support for the broader claims, as hemoglobin and mathemoglobin are not considered to exemplify any 'masking agent').

The claims are drawn to a method of suppressing the interference of a masking agent on a molecular assay of a nucleic acid containing test sample or a method of improving the signal response of a molecular assay by suppressing the interference of a masking agent on a molecular assay of a nucleic acid containing test sample comprising contacting the test sample with an amount of a divalent metal chelator and a chelator enhancing component. Claim 17 is further drawn to extracting molecular analytes of interest from the sample, and conducting a molecular assay on the extracted molecular analytes. It is noted that the claims are not drawn to

embodiments where the divalent metal chelator and chelator enhancing component are added together or in a solution.

Harvey et al teach and claim methods and devices for collecting, storing, and purifying nucleic acids such as DNA or RNA from fluid samples for subsequent genetic characterization by conventional amplification methods (see abstract, claims 1-34). Harvey et al specifically teach that the nucleic acids can be either from an untreated blood source such as saliva, serum or urine, or a treated blood source (see abstract, col. 2, lines 54-65) that has naturally occurring nucleic acid amplification inhibitors present, such as hemoglobin. Harvey et al teach that the device, 903 paper, should be composed of an absorbent material that does not bind nucleic acids irreversibly, impregnated with a chaotropic salt such as guanidine isothiocyanate or sodium perchlorate. Harvey et al specifically teach a method whereby a square of treated paper (treated with guanidine thiocyanate – see example 1, col. 5) is added to blood which has been collected in a tube containing EDTA (see example 6). Harvey et al teach that DNA was extracted from the paper and subjected to PCR (see figure 7, lanes 9 and 10 which show amplification of product). It is noted that Harvey et al does not teach suppressing the effects of methemoglobin, however such is considered a component of blood samples along with hemoglobin and other oxidation and breakdown products thereof. Hemoglobin was known to inhibit PCR reactions at the time of the invention. Further, such inhibition was known to be caused by heme (see Akane et al), which is a component of methemoglobin.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 7 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harvey et al.

Harvey et al teach and claim methods and devices for collecting, storing, and purifying nucleic acids such as DNA or RNA from fluid samples for subsequent genetic characterization by conventional amplification methods (see abstract, claims 1-34). Harvey et al specifically teach that the nucleic acids can be either from an untreated blood source such as saliva, serum or urine, or a treated blood source (see abstract, col. 2, lines 54-65) that has naturally occurring nucleic acid amplification inhibitors present, such as hemoglobin. Harvey et al teach that the device, 903 paper, should be composed of an absorbent material that does not bind nucleic acids irreversibly, impregnated with a chaotropic salt such as guanidine isothiocyanate or sodium perchlorate. Harvey et al specifically teach a method whereby a square of treated paper (treated with guanidine thiocyanate – see example 1, col. 5) is added to blood which has been collected in a tube containing EDTA (see example 6). Harvey et al teach that DNA was extracted from the paper and subjected to PCR (see figure 7, lanes 9 and 10 which show amplification of product). Harvey does not specifically exemplify paper treated with sodium perchlorate, however Harvey et al teach that such would be a suitable chaotropic agent. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the device of Harvey et al, treated with sodium perchlorate as Harvey et al teach that such would be a suitable device (see col. 3, lines 16-36) for use in the method of Harvey et al.

11. Claim 49 is rejected under 35 U.S.C. 103(a) as being unpatentable over Chung or Sigman, or Harvey et al (in the alternative), each in view of Ahern (The Scientist; vol. 9, pp 1-5- from the internet; 1995).

Chung et al teach an improved method of isolating quality polysaccharide free RNA from plant tissues by 1) adding an extraction buffer (buffer A) comprising 300 mM (0.3M) LiCl and 10mM (0.01M) EDTA and 1.5% SDS to a sample. Chung teaches performing RT-PCR on RNA isolated using said buffer.

Sigman teaches a method of isolating and preserving DNA. Sigman teaches that there is a need to isolate and prevent degradation of DNA in blood samples from patients suspected of infection with parasites, such as T. Cruzi (eukaryotic DNA) or other infectious agents during storage (p. 3, lines 16-19). Sigman teaches that isolation and storage comprise contacting a biological sample containing DNA in cells with a buffer (aqueous solution) containing a nonamphipathic chaotropic salt (chelator enhancing component) such as guanidine thiocyanate or guanidine chloride and a concentration of a chelating agent. Sigman teaches performing PCR with the preserved nucleic acid.

Harvey et al teach and claim methods and devices for collecting, storing, and purifying nucleic acids such as DNA or RNA from fluid samples for subsequent genetic characterization by conventional amplification methods (see abstract, claims 1-34). Harvey et al teach that the device, 903 paper, should be composed of an absorbent material that does not bind nucleic acids irreversibly, impregnated with a chaotropic salt such as guanidine isothiocyanate or sodium perchlorate. Harvey et al specifically teach a method whereby a square of treated paper (treated with guanidine thiocyanate – see example 1, col. 5) is added to blood which has been collected in

a tube containing EDTA (see example 6). Harvey et al teach that DNA was extracted from the paper and subjected to PCR.

Neither Chung nor Sigman nor Harvey et al teach the reagents or device in kit format, however Ahern teaches that providing reagents and products in kit offer scientists the opportunity to better manage their time, and that such kits are convenient. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to package the reagent of Chung or Sigman, or the device of Harvey et al in kit format for the purposes of providing premade reagents which are convenient and will save researchers time, as taught by Ahern.

Double Patenting

12. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 37-47 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 21-24 of copending application 09/805,785. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims are coextensive in scope. Claims 21-23 of the '785

application are drawn to the same subject matter as claims 37-47 of the instant application. Although each of claims 37-47 of the instant application are not identical in scope to the claims of the '785 application, the dependent claims of the instant application specify the same chelators, chelator enhancing components, and concentration ranges of the instantly pending claims. Further, with regard to instantly pending claim 37, it would have been prima facie obvious to the ordinary artisan to improve hybridization between a primer and target or test nucleic acid during an amplification reaction for the purposes of improving the efficiency of the amplification reaction.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

13. Claims 1-16 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 6,458,546. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims are coextensive in scope. The claimed method steps of the instant application encompass the more narrow methods steps of the claims of the '546 patent. The claims of the '546 patent do not recite a method of suppressing a masking agent, however, the claims are drawn to a method of preserving a nucleic acid in a bodily fluid by adding a reagent containing, for example, EDTA and guanidine thiocyanate to a bodily fluid. Guanidine thiocyanate is a chaotropic agent known to inhibit proteases, therefore, suppressing a masking agent such as a nuclease (which would mask the amount of nucleic acid in a sample by degrading it) is considered a property of the claimed method of the '546 patent.

14. Claims 17-36 and 48 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 6,458,546 in view of Sigman.

The instant claims are drawn to a method of improving the signal response of a molecular assay by interfering with a masking agent by adding a divalent metal chelator (further drawn to adding such in solution in the range of from about 0.001M to 0.1M) and a chelator enhancing component (further drawn to adding such in solution in the range of from about 0.1M to 2M) to a test sample, which can be a biological fluid, extracting molecular analytes of interest from the sample, and conducting a molecular assay on the extracted molecular analytes. Claims 1-8 of the '546 patent are drawn to preserving nucleic acids in a biological fluid by contacting the biological fluid with a solution containing a divalent metal chelator in the range of from about 0.001M to about 0.1M and a chelator enhancing component in the range of from about 0.1M to about 2M. Although the claims of the '546 patent do not disclose extracting the nucleic acids and conducting a molecular assay on the extracted nucleic acids, Sigman teaches a method of isolating and preserving DNA and extracting the isolated and preserved DNA to perform molecular assays, such as hybridization and PCR on the extracted DNA (p. 3, lines 16-19). Sigman specifically teaches that the DNA was extracted (extracting molecular analytes of interest) and electrophoresed (conducting a molecular assay) and T.cruzi nucleic acids were identified. Sigman teaches that there is a need to prepare the DNA for amplification (p. 3, lines 20-21). Sigman specifically teaches a polymerase chain reaction on cleaved minicircle DNA extracted from a blood/GnCl/ EDTA (GEB lysate) sample (see examples 3 and 4). Sigman teaches that using the GEB lysate, PCR amplification of extracted minicircles was sensitive enough that a single T.cruzi cell could be detected in 20 ml of blood (p. 35). Therefore, it would

have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to extract and assay the nucleic acids preserved in the claims of the '546 patent for the purpose of sequencing, or identifying the origin of the DNA preserved, for example to identify infective pathogens in a sample of blood from a patient as taught by Sigman. The ordinary artisan would have been motivated to extract and assay the nucleic acids preserved in the method of the '546 patent for the purpose of identifying such nucleic acids for diagnosing a pathogenic infection, for example. Guanidine thiocyanate is a chaotropic agent known to inhibit proteases, therefore, suppressing a masking agent such as a nuclease (which would mask the amount of nucleic acid in a sample by degrading it) is considered a property of the claimed method of the '546 patent.

15. Claim 49 is rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 6,458,546 in view of Ahern. Claims 1-8 of the '546 patent are drawn to preserving nucleic acids in a biological fluid by contacting the biological fluid with a solution containing a divalent metal chelator in the range of from about 0.001M to about 0.1M and a chelator enhancing component in the range of from about 0.1M to about 2M. Although the claims of the '546 patent do not disclose the preservative solution in kit format, Ahern teaches that providing reagents and products in kit offer scientists the opportunity to better manage their time, and that such kits are convenient. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to package the reagent of the '546 patent in kit format for the purposes of providing premade reagents which are convenient and will save researchers time, as taught by Ahern.

It is noted that the "use for" the kit carries no patentable weight. Guanidine thiocyanate is a chaotropic agent known to inhibit proteases, therefore, suppressing a masking agent such as a nuclease (which would mask the amount of nucleic acid in a sample by degrading it) is considered a property of the preservative solution recited in the claimed methods of the '546 patent.

Conclusion

16. No claims are allowable over the cited prior art.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Souaya whose telephone number is (703) 308-6565. The examiner can normally be reached Monday-Friday from 9:00 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Jehanne Souaya
Patent examiner
Art Unit 1634
Jehanne Souaya
April 14, 2002